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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

HAQ, SHAFIQL

ART UNIT PAPER NUMBER

1641

DATE MAILED: 10/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/524,207	EZAN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Shafiqul Haq	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 10 July 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>7/10/06</u> . | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. Applicants' responses and amendments filed July 10, 2006 is acknowledged and entered.
2. Claims 1-26 are pending and under active prosecution.
3. IDS submitted 7/10/06 has been considered and a signed copy is provided.

### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
6. With respect to Claim 1 the structure of the "silylated organic compound" is unclear i.e. chemical linkage of silyl group with the organic compound in the structure of "silylated organic compound" is unclear.
7. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: detecting and/or measuring step for the appearance of desilylated organic compound or disappearance of silylated organic compound.
8. With respect to claim 15, it is unclear what compound(s) or reagent(s) are encompassed by the term "a means for detecting" in the kit claim.
9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1 is again rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for organic compounds such as steroid, cytokines, estradiol etc., does not reasonably provide enablement for any organic compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

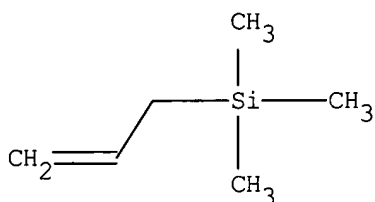
The specification provides guidance only for hydroxylated organic compounds attached to silane. Examples of silyl groups for silylating hydroxylated organic compounds is provided in page 8, lines 6-16 of specification. Page 6, lines 21-23 of specification recites "in order to be able to be silylated, this compound contains at least one hydroxyl function which is accessible for silylation". General principal of reaction of HF on Si-O bond is disclosed in page 6 (reaction scheme on top). The specification also provides examples of steroid, cytokines, estradiol attached to silane through oxygen atom as silylated compounds but there is no enablement in the specification for use of all silylated organic compound (i.e. organic compounds not linked through oxygen atom to silane group i.e. Si-O bond).

Trialkyl silyl (e.g. trimethyl silyl, triethyl silyl) are common alcohol protecting group. Organic compound having hydroxyl group are reacted with alkyl silyl to form a Si-O bond with the organic compound ( $R_3\text{-Si-O-organic compound}$ ) and a mild acid such as HF can remove organic group by attacking on oxygen atom. Therefore,

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a heteroatom (such as oxygen) is required for removing silyl group from the organic group. A silylated organic compound wherein organic compound (e.g. hydrocarbon chain) is linked to silicon atom of trimethyl silane through a carbon atom is not suitable for a nucleophilic substitution reaction with HF or fluoride ion.

As for example, silylated organic compound such as Allyltrimethyl silane as shown below is not enabled for detection of trace amount of HF in a sample:



Nucleophilic substitution reaction with fluoride will not readily occur to form a desilylated organic compound ( $\text{CH}_2=\text{CH}-\text{CH}_3$ ). Therefore, all compounds encompassed by the term "silylated organic compound" is not enabled.

The specification provides guidance and working examples only for silylated organic compound wherein organic compound is attached to silicon atom of silyl group through oxygen atom, but there is no enablement in the specification for silylated organic compounds wherein organic compounds are attached to silicon atom of silyl group through carbon atom or other heteroatom. In specification, there is not a single example wherein silane (Si) is attached to organic group other than oxygen atom. The desilylation activity of HF wherein organic compounds are attached to silicon atom of silyl group through carbon atom or other heteroatom will be different (i.e. may be much less) from the desilylation activity of HF wherein silylated organic compound wherein silyl is attached to organic compound through

oxygen atom. It may require presence of a much higher strength of fluoride in a sample for detection which may not be practical. Therefore, an artisan in the art would not be able to practice the invention because an undue experimentation will be required to judge suitability of other compounds (except SDS) for preparation of immunoassay calibrator as described above. Undue experimentation would be required to practice the invention as claimed due to the quantity of experimentation necessary; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and breadth of the claims. In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

### ***Claim Rejections - 35 USC § 102***

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1 is again rejected under 35 U.S.C. 102(b) as being anticipated by Descalzo et al (The journal of Royal Society of Chemistry, 2002).

Descalzo et al disclose a method for determination of fluoride in a sample (see abastact). Silylated organic compounds are disclosed (see scheme 1 of page 563) and the presence of fluoride in solution liberates organic compound from silica (i.e. desilylated organic compound). The method comprises bringing in contact, in

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solution, a fluoride sample with silylated organic compound and the liberated organic compound is measured which is indicative of the presence/or concentration of fluoride in a sample (page 562, lines 16-29 of left column and lines 33-45 of right column and scheme 1 of page 563). It is presumed that unsilylated compound (fluorophore) is also measured for comparison with the liberated organic molecule (fluorophore) (see fig. 1).

Therefore, the reference deems to anticipate the cited claims.

### ***Claim Rejections - 35 USC § 103***

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. Claim 15 is again rejected under 35 U.S.C. 103(a) as being unpatentable over Descalzo et al (The journal of Royal Society of Chemistry, 2002).

Descalzo et al disclose a method for determination of fluoride in a sample using Silylated organic compounds as described above in paragraph 13 but fail to disclose components compiled in a kit. However, the packaging of components in kit form is a well-known obvious expedient for ease and convenience in assay performance and once a method has been established, one skilled in the art would clearly consider

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compiling in a kit format and change/modify different components of the kit to best suit the assay.

15. Claims 15-26 are again rejected under 35 U.S.C. 103(a) as being unpatentable over each of 1) Salari (journal of chromatography, 1987, vol 416, pages 219-235) and 2) Tallent et al (Journal of lipid research, 1968, Vol 9, pages 146-148).

The method of use limitation in claim 15 do not affect the composition itself which is composed solely of two components, the silylated compound and the detection and therefore, the use limitation has not given any patentable weight.

Salari discloses silylated organic compounds (e.g. trimethylsilyl ester, tert-butylmethylsilyl esters) (see title and page 221) and detection by gas chromatography and mass spectrometry (see figs. 2-7).

Tallent et al. also disclose silylated organic compounds (e.g. silylated BSA) (page 147, left column under results and discussion) and detection by gas chromatography and mass spectrometry (see Fig.1).

Since, packaging of components in kit form is a well-known obvious expedient for ease and convenience in assay performance and once a method has been established, one skilled in the art would clearly consider compiling components in a kit format and change/modify different components of the kit to best suit the assay.



***Response to Argument***

16. Applicant's arguments filed 7/10/05 have been fully considered, and are persuasive to overcome some of the rejection under 35 USC 112, but they are not persuasive to overcome the rejections under 35 USC 102 and 35 USC 103.

With respect to claim 1 rejected under 35 U.S.C. 112, second paragraph, the rejection was not on the definiteness of the term "silylated organic compound". The rejection was based on the indefiniteness of the structural composition of claimed "silylated organic compound". Silylated organic compounds have two components, silyl group and an organic group. What is unclear is the structure of the "silylated organic compound" i.e. chemical linkage of silyl group with the organic compound in the structure of "silylated organic compound" is unclear.

With respect to "means for detecting" of claim 15, the claim is a composition claim and its unclear how this term "means for detection" fits in the component of this composition claim. The components of a composition claims should be clearly stated to make the claim definite. Is this "means for detecting" – a component of the claimed invention? If it is then what is this component?

With respect to enabling rejection under 35 USC 112 first paragraph, in last office action, the examiner cited language from specification (lines 21-23 of specification) which states that a in order to get a silylated organic compound, the organic compound should contain at least one hydroxyl function. Applicants argued that with the present specification in hand, the operability of the claimed invention for any organic compound including a silyl group whatever the rest of the organic molecule

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ma be. This is not persuasive and the examiner disagrees with this statement. Teaching of specification is limited to silyl group linked to organic compound through oxygen atom and one skilled artisan would not readily appreciate any silylated organic compound (i.e. organic compound linked to silyl group through carbon atom or other heteroatoms other than oxygen) without undue experimentation. An explanation why "all silylated organic compound" is not enabled is clearly stated in paragraph 9 of this office action.

With regard to 102(b) rejection, Descalzo et al. disclose reaction of silylated organic compound with fluoride sample in a solution. A suspension of silylated organic compound (attached to silica beads) in a buffer is reacted with fluoride sample. MPEP 2111.01 [R-3] states that the words of a claim must be given their "plain meaning" unless they are defined in the specification. The plain meaning of "homogeneous mixture" (Webster's II Dictionary) is a homogeneous mixture of two or more substances, which may be solids, liquids, gases, or a combination of these. An aqueous solution is defined as any solution in which water is the solvent. Therefore, considering dictionary meaning of "aqueous solution", Descalzo discloses organic compound used **in solution**.

With regard to 103 (a) rejection of kit claims 12-26 under Salari et al. and Tallent, the kit claim (claim 15) is a composition claim (i.e. product). Applicant is reminded that a recitation of the intended use of the claimed invention, i.e. "for detecting and measuring the concentration of fluoride(F) of hydrogen fluoride (HF) in a sample", must result in a structural difference between the claimed invention and the prior art

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in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Therefore, the intended use and method of use limitation (appearance or disappearance in the presence of HF) in claim 15 do not affect the composition itself which is composed solely of two components, the silylated compound and the detection means and therefore, the use limitation has not given any patentable weight. With regard to compiling components in a kit form, the packaging of components in kit form is a well-known obvious expedient for ease and convenience in assay performance and once a method has been established, one skilled in the art would clearly consider compiling components in a kit format and change/modify different components of the kit to best suit the assay.

### ***Conclusion***

17. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and

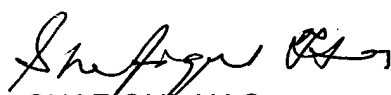
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any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

1. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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